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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/070,328	04/08/2004	Roberto Takashi Sudo	32390-178943	9691

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,328	SUDO ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 16-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 16-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on December 14, 2005.

Claims 1-11 and 16-27 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are under new grounds or necessitated by the amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instantly amended claim 20 recites "A chemical composition comprising the compound of claim 5 and a second peptide compound" wherein there is no support for the term "peptide compound" in the specification as filed. Applicant did not indicate where in the

specification this recitation finds support. The specification page 13, lines 6-10 discloses dipeptides and tripeptides as carrier molecules that can be combined with LASSBio-294 (i.e., the compound of formula (II)). The instantly recited term "peptide" however, is broader in scope when compared to the terms recited in the specification. The above insertion of the term is not described sufficiently to provide support for all of the chemical compositions contemplated by the instant claims.

2. Claims 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising the compound of claim 5 and a pharmaceutically acceptable carrier, does not reasonably provide enablement for a composition having the characteristic of producing at least 20% oral bioavailability of the compound. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claim 20 is drawn to "a chemical composition comprising the compound of claim 5 and a second peptide compound; said composition having the characteristic of producing at least 20% bioavailability of the compound when taken orally", for which there is insufficient enablement in the specification regarding the types of composition intended by the claim. In general compounds 'that increase the bioavailability of a compounds' are known as prodrugs. Applicant indicates that 'the scope of the invention includes creating a prodrug of LASSBio294 compound by combining with a carrier molecule to increase the bioavailability', however, there is no description of any such prodrugs of the compound or a method of preparation of the same. The specification does not provide any explanation regarding how the instantly recited characteristic for the composition to 'produce 20% oral bioavailability' is established. There is neither a procedure describing how such compositions are prepared nor examples that illustrate the recited activity. Further, the instant claims appear to be 'reach through' claims. Reach through claims, in general have a format drawn to a characteristic or functionality of the compound or composition and thereby reach through to all types of compositions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one of skill in the art to practice the invention.

As provided by the specification at page 13, lines 6-10, the instant claim appears to be drawn to a 'prodrug'. A prodrug as defined by Bundgaard (Design of Prodrugs) "is an inactive species, and therefore, once its job is completed, intact prodrug represents unavailable drug" (see page 1). Thus, an important requirement of prodrugs is that they be pharmacologically inactive. The scope of the term 'prodrugs' is quite broad. A state of the art reference, Silverman (The Organic Chemistry of Drug Design and Drug Action) teaches many strategies for making

prodrugs. Among them are polymer-bound prodrugs (pages 369-374), acyclic prodrugs which form heterocyclic compounds *in vivo* (page 360), conjugates consisting of two or more drug molecules which are cleaved into active drug molecules (page 377), amine precursors which are converted to amines *in vivo* (page 358), and drugs bound to a carrier via a linker (page 374). Applicant has neither described nor provided working examples for the combination of the invention compound with various types of 'second compound' or 'carrier molecule' intended by the instant claim language. These types of combinations do not depend on the novelty of the claimed compounds for patentability, but instead require separate inventive effort and are patentable over the claimed compounds. The disclosure therefore cannot rely on the state of the art in providing the necessary description of the types of 'chemical compositions' intended by the instant claims. None of the types of 'chemical compositions' recited in the claims were prepared by applicants or specifically suggested in the disclosure.

Further, the application already includes claims towards 'pharmaceutical composition for oral administration', comprising the compound and a carrier, see for example, claims 16-18. The instant claims recite 'a composition comprising the compound and second peptide compound' and the specification provides that 'dipeptides, tripeptides, or molecules absorbed in the intestine via transporter-mediated transport' as examples of the second peptide compound recited in the claim. First, the specification does not support the recitation of "peptide" compound generally because the term is broader than the terms 'dipeptides' and 'tripeptides' indicated therein. Next, the specification does not provide any direction towards what other types of 'molecules' are intended by the recitation. The relevant search in the state of the art did not reveal any such compositions having the instantly recited characteristic or activity and therefore, one of ordinary

skill in the art would have the burden of undue experimentation to prepare the claimed compositions.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 and 16-27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 1, it is recited that "A compound.... **and** pharmaceutically acceptable salts thereof", which is unclear because it is not clear if 'a compound or a salt thereof' is claimed **or** 'a **mixture** of a compound and the salt' is claimed. Amending the claim to read as -- A compound..... ~~and~~ or a pharmaceutically acceptable ~~salts~~ salt thereof -- would overcome the rejection.
2. Claim 6 recites "A method of preparing the chemical compound of claim 1 comprising steps of contacting 3,4-methylenedioxybenzoylhydrazine with an equimolar amount of thiophene-2-carboxaldehyde; and recovering the compound". The process recited is specific to the preparation of the compound of formula (II) and does not provide any reference to the preparation of the other compounds that fall within the genus of formula (I). Accordingly, the claim should be dependent on claim 5 and not claim 1.
3. The language of claim 7 will be in better form if it is amended to recite:

   -- The method according to claim 6, wherein said thiophene-2-carboxaldehyde is in a solvent and in the presence of a catalyst ~~is used~~ --.

4. In claim 9, the recitation "A method of treating congestive heart failure in a patient with a calcium sensitizer" is confusing. The claim appears to read on a "patient with a calcium sensitizer", which is not understood. The claim would be clear if it reads as: -- A method of treating congestive heart failure in a patient ~~with a calcium sensitizer~~, comprising ... -- . (The suggested claim language is consistent with newly added claims 26-27).
5. Claim 16 drawn to 'a pharmaceutical composition' does not recite -- a pharmaceutically acceptable carrier -- for the composition. (Claim language consistent with claims 22-25 is suggested).
6. Claim 17 recites: "The pharmaceutical composition of claim 16, further **comprising** pharmaceutically acceptable inactive ingredients, **comprising** ....", wherein the plural recitation of the term "ingredients" is not proper Markush language. Further, repetition of the term 'comprising' is redundant. Replacing the above recitation with -- The pharmaceutical composition of claim 16, further comprising **a** pharmaceutically acceptable inactive ~~ingredients comprising~~ **ingredient selected from**, -- improves the claim language. (***Note***: If claim 16 is amended to include 'a carrier', then the recitation of "carriers" in line 2 of claim 17 would be repetitive and redundant).
7. Claim 21 recites the limitation "The composition of claim 19 wherein the second peptide compound ...." in lines 1-2. There is insufficient antecedent basis for this limitation in claim 19 on which claim 21 is dependent. Claim 19 does not contain any recitation of 'a second compound'. Applicant may have intended to make claim 21 depend from claim 20.

8. Claims 26 and 27 are drawn to "A method of treating congestive heart failure", however, the claims do not contain a recitation that the method is towards treating congestive heart failure "**in a patient**". Appropriate amendment of the recitation in each of the claims as "A method of treating congestive heart failure in a patient" is suggested. (This suggestion is consistent with the language in claim 9, line 1).

Allowable Subject Matter

Claims 1-11, 16-19 and 22-27 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action. The references of record do not teach or fairly suggest the instantly claimed compounds.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

March 1, 2006